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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/838,785	04/20/2001	Ted Lau	51831AUSM1	9790

7590 07/12/2004

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/838,785	LAU ET AL	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 March 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☒ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *see attached Office action*.

3. ☒ Applicant's reply has overcome the following rejection(s): objection.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *NONE*.

Claim(s) objected to: *NONE*.

Claim(s) rejected: *28-29 for reasons already of record, because the amendment adding new claims 39-41 is not and will not be entered.*.

Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The amendment is not and will not be entered.

Applicant adds new claims 39-41. Claim 41 raises new issue, i.e. new matter, because the radioisotopes Sc47, Sc48, Ga72, Ga73, Cu67, Pd109, Arg11, Pm149, Ho166, Lu177, Re188, At211, Bi211-214 of claim 41 do not have support in the specification.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Claims 28-29 remain rejected under 35 USC 112, first paragraph, pertaining to lack of enablement for a method of selectively killing prostate cells or a method of treating prostate cancer, for reasons already of record of paper No:15, of 12/17/03.

Applicant argues that the Examiner clearly is saying that an in vivo example of treating prostate cancer is required in order for the specification to be enabling. Applicant recites *In re Brana*, stating that in vivo data is not necessary to support utility, and that the concerns raised by the Examiner are ones which would be addressed during the normal preclinical/clinical evaluation of a drug candidate.

Applicant asserts that Prost 03 is a prostate specific target, is a cell surface protein, and that the antibodies specific for Prost 03 stain prostate tumor tissue and prostate metastases.

Applicant recites the reference by Timme et al, 2003, stating that several clinical trials are underway, using radiolabeled antibody to prostate specific membrane antigen, or SGN-15, a doxyrubicin conjugated antibody to Lewis Y antigen that is highly expressed in prostate cancer.

Applicant argues that the Examiner has not shown any information that would make one doubt that PROST03 might be an equally useful therapeutic target, but merely brought up various issues that one would always encounter in the normal process of preclinal drug evaluation.

The recitation of Timme et al is acknowledged.

Applicant arguments have been considered but are found not to be persuasive for the following reasons:

Although in vivo data is not always required, however, in view of the unpredictability of cancer therapy, as overwhelmingly taught by WO93/17715, Gura, Hartwell, and Boon et al, all of record, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention.

The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Further, although there were many examples of immunoconjugates comprising antibodies and toxins being used to selectively kill cells, these examples are not applicable to the claimed invention, because different antibodies behave in vivo differently, and one cannot predict that the PROST 03 immunoconjugate used in the claimed method could be used successful in vivo for killing prostate cancer cells or for treating prostate cancer. This issue is clearly shown by White et al, who teach that for a successful immunotherapy, besides the specificity of the antigen, other following properties of the antigen should also be considered: The antigen should be present on all or near all of the malignant cells to allow effective targeting and to prevent a subpopulation of antigen-negative cells from proliferating. Further, antibodies have been developed against a broad spectrum of antigens, and whether the antigens shed, modulate or internalize influence the effectiveness of the administered antibody (p.126, second paragraph). Moreover, antigen internalization or downregulation can cause repeat dosing to be unsuccessful due to the disappearance of the antibody target (p.126, paragraph before last). Thus, although those skilled in the art at the time the invention was made were aware of these issues, these issues are inherent properties of the antigens, such as antigen shedding, modulating or internalization, and consequently

the inherent effectiveness of the immunoconjugate. Applicant however has not shown the properties of the antigens targeted by the antibodies used in the claimed method, such that one could predict the effectiveness of the immunoconjugate of the claimed method in targeting and preventing a subpopulation of antigen-negative cells from proliferating. Applicant has not addressed how to enhance the effectiveness of the immunoconjugate used in the claimed method, if the problem concerning the effectiveness of targeting exists. Thus since the properties or behavior of the antigens and the cancer cells to which the immunoconjugate of the claimed method are not known, it is unpredictable that the immunoconjugate used in the claimed method would effectively target cancer cells in adequate amount for a successful therapy in vivo.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

July 07, 2004